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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
WILSON, MICHAEL C	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 05/05/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/730,488	FRIEDMAN ET AL.	
	Examiner	Art Unit	
	Michael C. Wilson	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *54-61* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *54-61* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12-8-03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-53 have been canceled. Claims 54-61 have been added and are under consideration in the instant application.

Specification

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. **The sequences on page 116, lines 25 and 27; page 117, lines 1 and 3; page 123, line 19, pg 140-141, Table 3; page 142, lines 6 and 7; pg 142, Table 4; pg 143, line 6; page 149-150; and page 155-156; Fig. 22A (page 18, line 11); Fig. 21B (2 sequences); Fig. 21C (one sequence); Fig. 20A; Fig. 17 (2 sequences); Fig. 14 (3 sequences); Fig. 10 (2 sequences) require SEQ ID NO.** Applicants must file a "Sequence Listing" accompanied by directions to enter the listing into the specification as an amendment. Applicant also must provide statements regarding sameness and new matter with regards to the CRF and the "Sequence Listing." Applicant is requested to return a copy of the attached Notice to Comply with the reply. Failure to fully comply with the sequence rules in response to the instant office action will be considered non-responsive.

The descriptions of the drawings should begin as follows: Fig. 7A-7C (page 13), Fig. 11A and 11B, Fig. 12A and 12B, Fig. 15A and 15B, Fig. 18A and 18B, Fig. 19A and 19B, Fig. 20A-20C, Fig. 21A-21C, Fig. 22A and 22B, Fig. 23A and 23B, Fig. 24A-24C, Fig. 25A-25C, Fig. 26A and 26B, Fig. 28A-28F, Fig. 29A-29C, Fig. 32A and 32B, Fig. 34A and 34B.

The abstract of the disclosure is objected to because it is greater than 250 words. Correction is required. See MPEP § 608.01(b).

Priority

This application repeats a substantial portion of prior Application No. 08/485943, filed 6-7-95, and adds/claims additional disclosure not presented in the prior application. Since this application names an inventor or inventors named in the prior application, 09/736084 is a continuation-in-part of 08/485043. Should applicant desire to obtain the benefit of the filing date of the prior application, attention is directed to 35 U.S.C. 120 and 37 CFR 1.78. In particular, the preliminary amendment in the instant application is essentially the same as the preliminary amendment in parent application '084; however, the preliminary amendment filed in 09/736084 adds disclosures not originally present in 08/485943 as originally filed.

The limitation of administering an adenovirus encoding leptin intravenously was not contemplated in '943 as originally filed (claim 54 and 59).

The limitation of administering an adenovirus encoding leptin to a mammal having a deficiency in leptin was not contemplated in '943 as originally filed (claim 54 and 58).

The limitation of "leptin operably linked to a promoter" (claim 54) or "leptin operably linked to an expression control sequence" was not contemplated in '943 as originally filed (claim 57).

The limitation of expressing an adenoviral vector in the liver was not contemplated in '943 as originally filed (claim 55).

The limitation of a mammal exhibiting a decrease in serum glucose or insulin levels was not contemplated in '943 as originally filed because Table 11 in '943 did not state the glucose or insulin levels were obtained from the serum (54 and 57).

The limitation of administering an adenovirus encoding leptin to a mammal and obtaining a decrease in glucose or insulin was not contemplated in '943 as originally filed because Table 11 in '943 did not teach administering an adenovirus encoding leptin causes a decrease in glucose or insulin (54 and 57).

The limitation of performing the method in humans was not contemplated in '943 as originally filed (claims 56, 60 and 61).

The concept currently claimed was first introduced in new claims 54-65 in the preliminary amendment filed on 12-13-00, paper number 7, of parent application 09/736084 (and was introduced by preliminary amendment into the instant application). This was a year after the subject matter was disclosed in US Patent 6,001,816 on 12-14-99.

Accordingly, the instant application is a Continuation of 09/736084, which is a Continuation-in-part of US Application 08/485943 because the preliminary amendment

filed in the instant application and '084 claims concepts not previously contemplated in '943 as originally filed.

The amendment to the first line of the specification filed 12-8-03, has been entered but will need corrected to indicate 09/736084 is a CIP of 08/495943 and not a CON.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Written Description

Claims 54-61 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

If applicants establish 09/736084 is a Continuation of 08/485943, the effective filing date of the claimed invention is 6-7-95, the filing date of parent application 08/485943. The following written description rejection assumes the effective filing date of the claimed invention is 6-7-95, the filing date of parent application 08/485943.

The concept of any species of leptin as broadly encompassed by "a" leptin or "an" OB protein as claimed lacks written description. The specification does not provide adequate written description for "a" leptin (claim 54) or "an" OB protein (claim 57) as

broadly claimed. The specification only teaches the mouse and human leptin proteins, which were the only species of leptin known in the art at the time of filing. An adequate written description of a protein requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the protein itself in a representative number of species. It is not sufficient to define a protein solely by its principal biological property in mice and humans because disclosure of no more than that, as in the instant case, is simply a wish to know the identity of any leptin in other species having that biological property. Also, naming a type of material generically known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. Thus, claiming all a method using a vector encoding any leptin without defining a representative number of species of leptin is not in compliance with the description requirement. Rather, it is an attempt to preempt the future before it has arrived. (See *Fiers v. Revel*, 25 USPQ2d 1601 (CA FC 1993) and *Regents of the Univ. Calif. v. Eli Lilly & Co.*, 43 USPQ2d 1398 (CA FC, 1997)).

Enablement

Claims 54-61 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

If applicants overcomes the priority issue and establishes 09/736084 is a continuation of 08/485943, the effective filing date of the claimed invention is 6-7-95, the filing date of parent application 08/485943. The following enablement rejection assumes the effective filing date of the claimed invention is 6-7-95, the filing date of parent application 08/485943.

Breadth of the claims

Claim 54 is drawn toward a method of treating obesity in a mammal having a deficiency in functional leptin by administering intravenously to the mammal an adenoviral vector comprising a DNA sequence encoding a leptin operably linked to a promoter and expressing the DNA sequence, wherein the mammal exhibits a decrease in body weight, a decrease in serum glucose levels and/or a decrease in serum insulin levels.

Claim 57 is drawn toward a method of treating obesity in a mammal by administering to the mammal an adenoviral vector comprising a DNA sequence encoding an OB protein operably linked to an expression control sequence and expressing the DNA sequence, wherein the mammal exhibits a decrease in body weight, a decrease in serum glucose levels and/or a decrease in serum insulin levels.

The obese (ob) gene product is equivalent to the leptin gene product (Tartaglia, 1995, Cell, Vol. 83, pages 1263-1271; see abstract, line 1; see the instant application on pg 5, lines 5-16).

Claim 57 is broader than claim 54 because it does not require the mammal has a leptin deficiency or that the adenovirus is administered intravenously. Claims 58 and 59, however, are dependent upon claim 57 and add these limitations.

The leptin proteins in the claims include leptin proteins isolated from any species.

The body of the claim requires the body weight, serum glucose level or serum insulin level of the mammal is decreased. Therefore, administration of a vector encoding leptin or ob must decrease body weight, serum glucose level or serum insulin level to have an enabled use according to the specification.

State of the art regarding the ob gene/protein

Ob/ob mice with a homozygous disruption in the ob gene were known to be obese (pg 3, lines 3-6).

At the time of filing parent application 08/485943 on 6-7-95, it was unknown whether obese ob/ob mice correlated to obese humans with a gene mutation. Since then, Clayton (Arch. Dis. Child, 1998, Vol. 78, 278-284) taught that 5% of humans with obesity have an ob concentration lower than expected (pg 282, col. 1, line 20).

The specification states: "Because of the myriad factors that seem to impact body weight, it has not been possible to predict which factors and, more particularly, which homeostatic mechanisms is actually primarily determinative. Nonetheless, the apparent connections between the ob gene and the extent and characteristics of obesity have prompted the further investigation and elucidation that is reflected by the present application. It is the identification of the sequence of the gene and corresponding

peptide materials, to which the present invention following below directs itself." (pg 4, lines 14-20).

Thus, it was unpredictable whether ob/ob mice correlated to any obese human or to a gene disruption that occurred in humans.

At the time of filing parent application 08/485943 on 6-7-95, the art did not teach what tissue expressed the ob protein. Nor did the art teach in what tissues the ob protein mediated an effect. After filing '943, Tartaglia (cited above, Dec. 29, 1995, Cell, Vol. 83, pages 1263-1271) confirmed that the tissue in which the ob protein mediated an effect remained unknown throughout 1995 (pg 1263, col. 2, line 2).

Thus, the tissue target required to express ob or to mediate a decrease in body weight in a mammal was unknown at the time of filing parent application 08/485943.

Unpredictability of gene therapy

At the time of filing parent application 08/4885943 (6-7-95) and since, the combination of vector, promoter, dosage, target tissue, level of expression and route of administration required to target the desired tissue so that a therapeutic would occur was unpredictable.

Feldman (Fundamental & Clinical Pharmacology, 1995, Vol. 9, pg 8-16) suggested treating restenosis using a vector encoding a protein. Feldman discussed experiments in which the vector administered to the arterial wall during angioplasty allowed low levels of protein expression in cells of the arterial wall. Feldman taught that obtaining a therapeutic effect was prevented by low numbers of cells expressing a transgene, transfection efficiency, target specificity, and sustained expression (pg 12,

"Arterial gene therapy"). None of the experiments described by Feldman resulted in a therapeutic effect.

Miller (Feb. 1995, FASEB J., Vol. 9, pg 190-199) reviewed the types of vectors available for *in vivo* gene therapy, and concluded that "for the long-term success as well as the widespread applicability of human gene therapy, there will have to be advances...targeting strategies outlined in this review, which are currently only at the experimental level, will have to be translated into components of safe and highly efficient delivery systems" (pg 198, col. 1). Miller did not obtain a therapeutic effect using gene delivery.

Crystal (Oct. 20, 1995, Science, Vol. 270, pg 404-410) also reviewed various vectors known in the art and indicates, "among the design hurdles for all vectors are the need to increase the efficiency of gene transfer, to increase target specificity and to enable the transferred gene to be regulated" (pg 409). Crystal did not obtain a therapeutic effect using gene delivery.

Verma (Sept. 1997, Nature, Vol. 389, pg 239-242) reviewed vectors for use in gene therapy and discussed problems associated with adenoviral vectors and indicates a resolution to vector targeting has not been achieved in the art (see entire article). Verma also taught appropriate regulatory elements may improve expression, but it is unpredictable what regulatory elements target what tissues (pg 240, sentence bridging col. 2-3). Verma did not obtain a therapeutic effect using gene delivery.

Deonarain (1998, Expert Opin. Ther. Pat., Vol. 8, pg 53-69) indicated that one of the biggest problems hampering successful gene therapy is the "ability to target a gene

to a significant population of cells and express it at adequate levels for a long enough period of time" (page 53, first paragraph). Deonarain reviewed new techniques under experimentation in the art that show promise but stated that such techniques were even less efficient than viral gene delivery that failed to work (see pg 65, 1st ¶ under "Conclusion"). Deonarain did not obtain a therapeutic effect using gene delivery.

Ross (Sept. 1996, Human Gene Therapy, Vol. 7, pg 1781-1790) stated a major technical impediment to gene transfer is the lack of ideal gene delivery systems including vectors, promoters and modes of delivery (pg 1782, col. 2, 1st full ¶). The ability to use gene therapy to obtain a therapeutic effect in a patient was unpredictable (Ross, pg 1789, col. 1, 1st ¶). Ross did not obtain a therapeutic effect using gene delivery.

Therefore, it was unpredictable what combination of vector, promoter, dosage, cells, level of expression and route of administration would provide a therapeutic effect using gene delivery at the time of filing parent application (6-7-95).

More specific to the claimed invention, and since the time of filing, Fletcher (Nov. 15, 1995, Blood, Vol. 86, page 241a) taught decreasing the body weight of an obese mouse having a homozygous mutation in the ob gene by administering bone marrow from an autologous mouse transduced with a retroviral vector encoding ob to the bone marrow of the recipient mouse (page 241a, line 12).

Morsy (1998, Proc. Natl. Acad. Sci., USA, Vol. 95, pages 7866-7871) taught that 60% weight loss can be obtained for 6-7 weeks following administration of a leptin-encoded adenoviral vector (pg 7870, col. 1, line 13); however, analysis revealed

eventual loss of the vector DNA 4 and 8 weeks following administration of the vector (pg 7870, col. 2, line 5).

Muzzin (PNAS, Dec. 1996, Vol. 93, pg 14804-14808) obtained weight loss of ob/ob mice by administering 3 x 10^9 particle forming units of helper adenoviral vector encoding leptin via the tail vein (pg 14805, ¶ bridging col. 1-2 and col. 2, 1st full ¶).

Teachings of the specification

Pg 5, line 8 teaches the "leptin" protein is absent in plasma of ob/ob mice. The specification does not teach the leptin protein is absent in obese humans.

The specification on pg 73-83 describes protein-based therapy for obesity. On pg 74, lines 25-28, applicants describe administering the ob protein by intravenous, intraarterial, intraperitoneal, intramuscular or subcutaneous routs of administration. Pg 83, line 17, through pg 84, line 5, describes administering the ob gene using a vector to decrease body weight of a mammal. The description of nucleic acid-based therapies on pg 83 does not include a description of the conditions required to obtain expression of the protein or the route of administration. The disclosure on pg 74 is limited to protein administration and does not include vector administration. One of skill in the art would not read the description of routes of administration for proteins on pg 74 as applying to the nucleic acid-based therapy on pg 83 because they are under different headings (see headings for "Polypeptide-based therapeutic treatment" and "Nucleic acid-based therapeutic treatments" on pg 73 and 83, respectively). The specification does not

teach any specific dosages or routes of delivery for the vectors listed for use in *in vivo* gene delivery.

Pg 83, line 17, teaches the ob gene can be "introduced into human fat cells to develop gene therapy for obesity." The specification does not teach how to target vectors to adipocytes using *in vivo* gene delivery. The specification does not teach what cells mediate the function of the ob protein so that one of skill could target a vector encoding ob to those cells.

Pg 83, line 21, through pg 84, line 12, lists viral vectors for delivering the ob gene. For example, defective viral vectors allow, "for administration to cells in a specific, localized area, without concern that the vector can infect other cells. Thus, adipose tissue can be specifically targeted." Such vectors include HSV, papillomavirus, EBV adenovirus, AAV and retrovirus. Pg 84, lines 13-28, describes introducing a vector by lipofection. Pg 85, lines 3-10, describe administering the vector as naked DNA plasmid. The specification does not teach the specific combination of vector, promoter, route of administration and dosage required to obtain ob expression in a mammal such that a decrease in body weight is obtained.

Pg 91 begins the examples section, which include gene mapping of the mouse and human ob gene, cloning of the mouse and human ob gene, preparing the ob protein, preparing antibodies to the ob protein and recombinant expression of the ob protein in bacteria.

Pg 119, line 24, through pg 125, line 26, and pg 126, Table 1, teach administering the ob protein to three strains of ob/ob mice. The ob/ob mice lost weight.

Pg 130, Example 9, and pg 137, Example 10, describe increased expression of ob in adipocytes as compared to other tissues. Since the time of filing, it has been confirmed that ob was expressed exclusively in adipose tissue (Clayton, cited above, pg 282, col. 1, line 3).

Pg 121, lines 1-27, describe the ob serum levels in mice and humans.

Pg 146, Example 11, teaches the human ob protein is active in ob/ob mice.

The specification teaches delivering ob protein to treat obesity on pg 73-74 but does not provide adequate guidance for one of skill to obtain the same serum level ob using gene delivery.

The specific combination of elements described by Fletcher, Morsy or Muzzin required to administer a vector encoding leptin to treat obesity in a mammal was not taught in application 08/485943 as originally filed 6-7-95.

Rejection

Overall, the specification does not overcome the unpredictability in the art by teaching the specific combination of vector, promoter, dosage and route of administration required to target ob expression to fat cells or how to express ob protein so it will target the tissue that mediates a reduction in body weight.

Fletcher (cited above) decreased the body weight of an obese mouse having a homozygous mutation in the ob gene by administering bone marrow from an autologous mouse transduced with a retroviral vector encoding ob to the bone marrow of the recipient mouse (page 241a, line 12). In view of the unpredictability in the art of gene therapy, the specific combination of retrovirus, transduced bone marrow cells and bone

marrow administration is essential to the invention. Applicants do not enable the claimed invention because applicants do not describe the specific combination of retrovirus, transduced bone marrow cells and bone marrow administration, which is essential to reduce body weight as taught by Fletcher.

Morsy (cited above) obtained weight loss by administering 1-2 x 10^{11} particles of helper adenoviral vector encoding leptin via the tail vein of ob/ob mice (pg 7869, col. 2; pg 7870, Fig. 4B, Fig. 5B, col. 1). In view of the unpredictability in the art of gene therapy, the specific combination of adenovirus, tail vein injection and the dosage of 1-2 x 10^{11} particles is essential to the invention. Given the state of the art regarding the ob gene/protein taken with the teachings in the specification, one of skill would not have expected intravenous administration to cause ob expression in adipocytes as contemplated by applicants as being the source of ob expression. Nor would one of skill have known that intravenous administration would cause ob expression capable of targeting cells that mediate a therapeutic effect. Applicants do not enable the claimed invention because the specification does not describe the specific combination of adenovirus, tail vein injection and the dosage of 1-2 x 10^{11} particles, which is essential to reduce body weight as taught by Morsy.

Muzzin (cited above) obtained weight loss of ob/ob mice by administering 3 x 10^{9} particle forming units of helper adenoviral vector encoding leptin via the tail vein (pg 14805, ¶ bridging col. 1-2 and col. 2, 1st full ¶). In view of the unpredictability in the art of gene therapy, the specific combination of adenovirus, tail vein injection and the dosage of 3 x 10^{9} pfu is essential to the invention. One of skill would not have expected

that intravenous administration would cause expression in adipocytes as contemplated by applicants as the source of the majority of ob expression. Nor would one of skill have expected that intravenous administration would cause ob expression capable of targeting cells capable of mediating a decrease in body weight. Applicants do not enable the claimed invention because the specification does not describe the specific combination of adenovirus, tail vein injection and the dosage of 3×10^9 pfu, which is essential to reduce body weight as taught by Muzzin.

In view of the art recognized unpredictability in gene therapy and the mere list of possible vectors provided by applicants on pg 83 and 84 without teaching the route of administration or dosage, those of skill in the art would be left to perform an undue amount of experimentation to determine the specific combination of vector, promoter, route of administration and dosage required to reduce body weight in a mammal.

In addition, the claims encompass administering a vector encoding ob and obtaining any body weight modulation. However, the specification is clearly limited to administering a vector encoding ob to decrease body weight (pg 83, line 18). Therefore, the claims should be limited to decreasing body weight.

Furthermore, the claims encompass decreasing the body weight of any mammal using a vector encoding an ob protein. However, the specification and the art since the time of filing are limited to treating mammals with an ob deficiency with the ob protein. The specification does not correlate the obese mammals having a defective ob gene to any other obese mammals or any other obesity related gene defect. The specification does not provide an enabled use for decreasing the body weight of a wild-type mammal

(having a normal weight). Therefore, it would require one of skill undue experimentation to determine how to use the vector encoding ob to treat obesity in any mammal as broadly claimed other than those with a defective ob gene.

The specification does not enable using a vector encoding any leptin or ob protein as broadly encompassed by claims 54 and 57. Salvador (Exp. Opin. Pharmacotherapy, 2001, Vol. 2, No. 10, pg 1615-1622) taught leptin is 167 amino acids in length and has the body weight control functions confined to amino acids residues 106-140. The specification teaches the conservative and non-conservative substitutions between the mouse and human leptin proteins in Fig. 4. The specification does not define what they consider "conservative" and "non-conservative" substitutions. The specification does not teach the functional region of the leptin protein or that any substitution as broadly claimed will allow the leptin protein produced to control body weight. Without such guidance it would have required one of skill undue experimentation to determine which amino acids could be substituted without altering the active site of leptin or to determine which amino acids could be substituted without altering the structure of the active site or the function of leptin.

Indefiniteness

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 54-61 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 54 and 57 are indefinite because it is unclear if the mammal exhibits a decrease in body weight, glucose level or insulin level before or after the adenovirus is administered. It is unclear if the mammal being treated has these characteristics or if these characteristics are a result of administering the adenovirus.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (f) he did not himself invent the subject matter sought to be patented.

Claims 54-61 are rejected under 35 U.S.C. 102(f) because the applicant did not invent the claimed subject matter.

Morsy (US Patent 6,001,816, Dec. 14, 1999) taught administering an adenoviral vector encoding leptin operably linked to a promoter to a mammal having a deficiency in functional leptin. The vector was administered intravenously and a decrease in weight, serum glucose and insulin levels were obtained (claims 1-3). In the response filed in 09/736084 on 12-13-00, paper number 7, applicants canceled the original claims and added new claims 54-65 directed toward administering an adenoviral vector encoding leptin operably linked to a promoter to a mammal having a deficiency in functional leptin intravenously such that a decrease in weight, serum glucose and insulin levels was

obtained. Applicants did not disclose the claimed subject matter until after the Morsy Patent issued. Applicants did not teach administering adenoviral vector intravenously such that a decrease in weight, serum glucose or serum insulin levels occurred. Given the unpredictability in the art taken with the teachings in the instant specification, the instant specification did not provide an enabling disclosure for the method claimed for reasons cited above. The preliminary amendment in the instant application filed 12-8-03 is based on the combination of elements discovered by Morsy required to treat obesity using an adenoviral vector encoding leptin.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 54-61 are rejected under 35 U.S.C. 102(e) as being anticipated by Morsy (US Patent 6,001,816, Dec. 14, 1999).

The effective filing date of the claimed invention is 12-8-03, the filing date of the instant application. Parent application 09/736084 as originally filed did not contemplate the claimed invention (see Priority section above).

Morsy taught administering an adenoviral vector encoding leptin operably linked to a promoter to a mammal having a deficiency in functional leptin. The vector was administered intravenously and a decrease in weight, serum glucose and insulin levels were obtained (claim 1). The leptin is expressed in the liver (claim 2) and the mammal is a human (claim 3).

Conclusion

No claim is allowed.

Inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Wilson who can normally be reached at the office on Monday, Tuesday, Thursday and Friday from 9:30 am to 6:00 pm at 571-272-0738.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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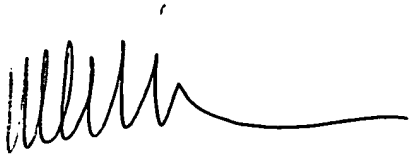
If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached on 571-272-0735.

The official fax number for this Group is (571) 273-8300.

Michael C. Wilson



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PRIMARY EXAMINER